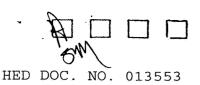
US ERA ARCHIVE DOCUMENT



POPHOOGEY

MEMORANDUM

July 7, 1999

SUBJECT:

Atrazine TM Quantitative Risk Assessment (Q_1^*) Based On Sprague-Dawley Female Rat Chronic Dietary Studies Using

mg/kg b.w.^3/41s/day Cross-Species Scaling Factor

P.C. Code 080803

TO:

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FATIVED

FROM:

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THROUGH:

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The most potent unit risk, $Q_1^*(mg/kg/day)^{-1}$, of those calculated for Atrazine is that for the Morseth study (1998) female rat mammary gland adenoma and/or carcinoma combined tumor rates at 1.12 x 10^{-1} in human equivalents. The dose levels used from the 105-week dietary study were 0, 25, 50, 70, and 400 ppm. The corresponding tumor rates were 12/80, 18/80, 21/79, 14/80, and 27/80, respectively.

Background

On September 10, 1987, the Carcinogenicity Peer Review Committee classified Atrazine as a category C carcinogen (possible human carcinogen) and recommended that a quantitative risk assessment be estimated for mammary gland tumors in female rats (Peer Review of Atrazine, J.W. Hauswirth, 3/1/88). A quantitative risk assessment (ATRAZINE - Updated Qualitative and Quantitative Risk Assessment from a Rat 2-Year Chronic Oral Toxicity/Oncogenicity Study, C.J. Nelson, 8/23/88) was prepared using the 2/3's scaling factor. This revised quantitative risk assessment reflects the Division change from use of

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the $^2/_3$'s to the $^3/_4$'s scaling factor in 1994¹.

Considering both chronic rat studies submitted to the agency to date, the most potent unit risk, Q_1^* , will be used for further calculations by the Agency. In this case, the most potent unit risk, Q_1^* , is that for the Morseth study (1998) female rat mammary gland adenoma and/or carcinoma combined tumor rates at 1.12 x 10^{-1} in human equivalents.

All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)\(^1\). For the conversion to human equivalents, weights of 0.35 kg for the rat and 70 kg for humans were used.

It is to be noted that the Q_1^* (mg/kg/day)⁻¹ is an estimate of the <u>upper bound</u> on risk and that, as stated in the EPA Risk Assessment Guidelines, "the true value of the risk is unknown, and may be as low as zero."

Dose-Response Analysis

The statistical evaluation of mortality (ATRAZINE - Updated Qualitative and Quantitative Risk Assessment from a Rat 2-Year Chronic Oral Toxicity/Oncogenicity Study, C.J. Nelson, 8/23/88, and Atrazine Qualitative Risk Assessment Based On Female Sprague-Dawley Rat Dietary Study, L. Brunsman, 2/9/99) indicated significant increasing trends with increasing doses of Atrazine in female rats of both the Mayhew (1986) and Morseth (1998) studies. Therefore, the estimates of unit risk, Q_1^* , for female rats were obtained by the application of the time-to-tumor Weibull model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Female rats of the Morseth study (1998) had significant increasing trends, and significant differences in the pair-wise comparisons of the 400 ppm dose group with the controls, for mammary gland carcinomas and adenomas and/or carcinomas combined, all at p < 0.01. There was also a significant pair-wise comparison of the 50 ppm dose group with the controls for mammary gland adenomas and/or carcinomas combined at p < 0.05.

Female rats of the Mayhew study (1986) had significant increasing trends, and significant differences in the pair-wise comparisons of the 1000 ppm dose group with the controls, for mammary gland adenocarcinomas, adenomas and/or adenocarcinomas combined and adenomas and/or adenocarcinomas and/or carcinosarcomas combined, all at p <

¹See memo - Deriving Q_1 *s Using the Unified Interspecies Scaling Factor, P.A. Fenner-Crisp, Director, HED, 7/1/94.

0.01. There were also significant pair-wise comparisons of the 70 and 500 ppm dose groups with the controls for mammary gland adenocarcinomas, adenomas and/or adenocarcinomas combined and adenomas and/or adenocarcinomas and/or carcinosarcomas combined, all at p < 0.05. When the 1000 ppm dose group is excluded from the analyses, female rats of the Mayhew study (1986) had significant increasing trends, and significant differences in the pair-wise comparisons of the 70 and 500 ppm dose groups with the controls, for mammary gland adenocarcinomas, and adenomas and/or adenocarcinomas combined, all at p < 0.05.

Additional Q1* Calculations

The unit risk, Q_1^* (mg/kg/day)⁻¹, of Atrazine based upon the Mayhew study (1986) female rat mammary gland adenoma and/or adenocarcinoma combined tumor rates is 6.44 x 10^{-2} in human equivalents. The dose levels used from the 106-week dietary study were 0, 10, 70, 500, and 1000 ppm. The corresponding tumor rates were 16/87, 16/67, 27/69, 27/68, and 45/88, respectively.

The unit risk, Q_1^* (mg/kg/day)⁻¹, of Atrazine based upon the Mayhew study (1986) female rat mammary gland adenoma and/or adenocarcinoma and/or carcinosarcoma combined tumor rates is 6.83 x 10^{-2} in human equivalents. The dose levels used from the 106-week dietary study were 0, 10, 70, 500, and 1000 ppm. The corresponding tumor rates were 16/87, 16/67, 27/69, 27/68, and 47/88, respectively.

When the 1000 ppm dose group is excluded from the analyses, the unit risk, Q_1^* (mg/kg/day)⁻¹, of Atrazine based upon the Mayhew study (1986) female rat mammary gland adenoma and/or adenocarcinoma combined tumor rates is 8.05×10^{-2} in human equivalents. The dose levels used from the 106-week dietary study were 0, 10, 70, and 500 ppm. The corresponding tumor rates were 16/87, 16/67, 27/69, and 27/68, respectively.